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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,483	07/25/2003	Ye Wu	X-0219	4224
7590 07/20/2005			EXAMINER	
Eric P. Mirabel BioNumerik Pharmaceuticals, Inc. Suite 1250 8122 Datapoint Drive San Antonio, TX 78229			MCKENZIE, THOMAS C	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 07/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	Application No. 10/627,483	Applicant(s) WU ET AL.	
	Examiner Thomas McKenzie, Ph.D.	Art Unit 1624	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 23 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_  
Claim(s) objected to: \_\_\_\_\_  
Claim(s) rejected: 3-5 and 8-11.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☒ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s) \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
Thomas C. McKenzie, Ph.D.  
Primary Examiner  
Art Unit: 1624

Continuation of 5. Applicant's reply has overcome the following rejection(s): THE INDEFINITENESS REJECTIONS MADE IN POINTS #4-#8 AND THE ENABLEMENT REJECTIONS MADE IN POINT #9 OF THE FINAL REJECTION. However, the amendment used to overcome point #6, the lack of a reduction step, has also introduced new matter.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 3-5 and 8-11 are newly rejected under paragraph 1 because the final sentence in claim 3 does not appear in the specification as filed and is new matter. The declaration by Harry Kochat is both too late and not persuasive for five reasons. Firstly, Applicants are comparing apples with oranges in their attempt to show an increased yield. The phosphonate compound used for the Horner reaction, which has an increased yield, has a carbomethoxy radical as radical R4. The compound used in the Wittig process, which has the lower yield, has a far more complex aspartyl ester radical as radical R4. Such a radical would be expected to give lower yields because of the added functionality leading to more possible side reactions. Secondly, the carbomethoxy compound has  $X = OCH_3$ , yet the presently claimed scope of X is far broader. The evidence is not commensurate in scope with the claims. Thirdly, an increase in yield from 73% to 83% is a change in degree not a change in kind. Fourthly, the ease of work-up in the Horner process, which avoids any triphenylphosphine oxide by product, is well known in the synthetic chemical arts. Triphenylphosphine oxide is notorious for being bulky, difficult to remove, and for appearing in every chromatographic fraction. Thus, the easier workup in a process, which does not involve this by-product, is hardly unexpected. Fifthly, Kochat admits the two reaction presented in his declaration are "based on results from the literature" but fails to state where in the original chemical literature these data may be found.

TCEU 7/16/05